

WHAT IS CLAIMED IS:

1. A method of reducing the risk of cataract development in a mammal comprising administering to the mammal an effective amount of a tetracycline derivative.
2. A method according to Claim 1, wherein said tetracycline derivative is a non-antimicrobial tetracycline.
3. A method according to Claim 1, wherein said tetracycline derivative is a dedimethylaminotetracycline.
4. A method according to Claim 3, wherein said dedimethylaminotetracycline is selected from the group consisting of 4-dedimethylaminotetracycline, 4-dedimethylamino-5-oxytetracycline, 4-dedimethylamino-7-chlorotetracycline, 4-hydroxy-4-dedimethylaminotetracycline, 5a,6-anhydro-4-hydroxy-4-dedimethylaminotetracycline, 6 α -deoxy-5-hydroxy-4-dedimethylaminotetracycline, 6-demethyl-6-deoxy-4-dedimethylaminotetracycline, 4-dedimethylamino-12a-deoxytetracycline, 12 α -deoxy-4-deoxy-4-dedimethylaminotetracycline, 12a, 4 α -anhydro-4-dedimethylaminotetracycline, 7-dimethylamino-6-demethyl-6-deoxy-4-dedimethylaminotetracycline, 5-hydroxy-6- α -deoxy-4-dedimethylaminotetracycline, 4-dedimethylamino-12 α -deoxyanhydrotetracycline and 4-dedimethylamino-11-hydroxy-12a-deoxytetracycline.
5. A method according to Claim 1, wherein said tetracycline derivative is 6 α -deoxy 5-hydroxy 4-dedimethylamino tetracycline.
6. A method according to Claim 1, wherein said tetracycline derivative is selected from the group consisting of 6a-benzylthiomethylenetetracycline, tetracyclinotrile, the mono-N-alkylated amide of tetracycline, 6-fluoro-6-demethyltetracycline, 11a-chlorotetracycline, tetracycline pyrazole, and 12a-deoxytetracycline and its derivatives.

7. A method according to Claim 1, wherein said tetracycline derivative is an antimicrobial tetracycline.

8. A method according to Claim 7, wherein said tetracycline derivative is tetracycline.

9. A method according to Claim 7, wherein said tetracycline derivative is minocycline.

10. A method according to Claim 7, wherein said tetracycline derivative is doxycycline

11. A method according to Claim 1, wherein said tetracycline derivative is administered systemically.

12. A method according to Claim 11, wherein said tetracycline derivative is administered systemically by a controlled release delivery system.

13. A method according to Claim 1, wherein said tetracycline derivative is administered orally.

14. A method according to Claim 1, wherein said tetracycline derivative is administered topically.

15. A method according to Claim 1, wherein said tetracycline derivative is a tetracycline compound of the formulae:

Structure A	or	Structure B
Structure C	or	Structure D

wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

10

R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;

R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, diazonium, di(lower alkyl)amino and $\text{RCH}(\text{NH}_2)\text{CO}$;

15

R is hydrogen or lower alkyl; and pharmaceutically acceptable and unacceptable salts thereof; with the following provisos:

when either R7 and R9 are hydrogen then R8 must be halogen; and

when R6-a, R6, R5 and R9 are all hydrogen and R7 is hydrogen, amino, nitro, halogen, dimethylamino or diethylamino, then R8 must be halogen; and

20

when R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is hydrogen, amino, nitro, halogen or diethylamino, then R8 is halogen; and

when R6-a is methyl, R6 is hydroxyl, R5, R7 and R9 are all hydrogen, then R8 must be halogen; and

25

when R6-a, R6 and R5 are all hydrogen, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

when R6-a is methyl, R6 is hydrogen, R5 is hydroxyl, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

when R6-a is methyl, R6, R5 and R9 are all hydrogen and R7 is cyano, then R8 must be halogen.

16. A method according to Claim 1, wherein said tetracycline derivative is a tetracycline compound of the formulae:

Structure E

or

Structure F or

Structure G

or

Structure H

5

wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, and di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;

R4 is selected from the group consisting of NOH, N-NH-A, and NH-A, where A is a lower alkyl group;

R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, di(lower alkyl)amino and $\text{RCH}(\text{NH}_2)\text{CO}$;

R is hydrogen or lower alkyl; and pharmaceutically acceptable and unacceptable salts thereof; with the following provisos:

when R4 is NOH, N-NH-alkyl or NH-alkyl and R7, R6-a, R6, R5, and R9 are all hydrogen, then R8 must be halogen; and

when R4 is NOH, R6-a is methyl, R6 is hydrogen or hydroxyl, R7 is halogen, R5 and R9 are both hydrogen, then R8 must be halogen; and

when R4 is N-NH-alkyl, R6-a is methyl, R6 is hydroxyl and R7, R5, R9 are all hydrogen, then R8 must be halogen; and

when R4 is NH-alkyl, R6-a, R6, R5 and R9 are all hydrogen, R7 is hydrogen, amino, mono(lower alkyl)amino, halogen, di(lower alkyl)amino or hydroxyl, then R8 must be halogen; and

when R4 is NH-alkyl, R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is mono(lower alkyl)amino or di(lower alkyl)amino, then R8 must be halogen; and

when R4 is NH-alkyl, R6-a is methyl, R6 is hydroxy or hydrogen and R7, R5, and R9 are all be hydrogen, then R8 must be halogen.

17. A method according to Claim 1, wherein said tetracycline derivative is a 4-dedimethylaminotetracycline compound having general formulae (I) through (IV):

General Formula (I)

Structure I

5 wherein: R7, R8, and R9 taken together in each case, have the following meanings:

	R7	R8	R9
	azido	hydrogen	hydrogen
	dimethylamino	hydrogen	azido
	hydrogen	hydrogen	amino
10	hydrogen	hydrogen	azido
	hydrogen	hydrogen	nitro
	dimethylamino	hydrogen	amino
	acylamino	hydrogen	hydrogen
	hydrogen	hydrogen	acylamino
15	amino	hydrogen	nitro
	hydrogen	hydrogen	(N,N-dimethyl)glycylamino
	amino	hydrogen	amino
	hydrogen	hydrogen	ethoxythiocarbonylthio
	dimethylamino	hydrogen	acylamino
20	dimethylamino	hydrogen	diazonium
	dimethylamino	chloro	amino
	hydrogen	chloro	amino
	amino	chloro	amino
	acylamino	chloro	acylamino
25	amino	chloro	hydrogen
	acylamino	chloro	hydrogen
	mono alkylamino	chloro	amino
	nitro	chloro	amino
	dimethylamino	chloro	acylamino
30	dimethylamino	chloro	dimethylamino

and

General Formula (II)

Structure J

or

Structure K or

Structure L

or

Structure M

35 wherein: R7, R8, and R9 taken together in each case, have the following meanings:

	R7	R8	R9
	azido	hydrogen	hydrogen
	dimethylamino	hydrogen	azido
	hydrogen	hydrogen	amino
40	hydrogen	hydrogen	azido
	hydrogen	hydrogen	nitro
	dimethylamino	hydrogen	amino
	acylamino	hydrogen	hydrogen
	hydrogen	hydrogen	acylamino
45	amino	hydrogen	nitro
	hydrogen	hydrogen	(N,N-dimethyl)glycylamino
	amino	hydrogen	amino
	hydrogen	hydrogen	ethoxythiocarbonylthio
	dimethylamino	hydrogen	acylamino
50	hydrogen	hydrogen	diazonium
	hydrogen	hydrogen	dimethylamino
	diazonium	hydrogen	hydrogen
	ethoxythiocarbonylthio	hydrogen	hydrogen
	dimethylamino	chloro	amino
55	amino	chloro	amino
	acylamino	chloro	acylamino
	hydrogen	chloro	amino
	amino	chloro	hydrogen
	acylamino	chloro	hydrogen
60	mono alkyl amino	chloro	amino
	nitro	chloro	amino

and

General Formula (III)

Structure N

65 wherein: R8 is hydrogen or halogen and R9 is selected from the group consisting of nitro, (N,N-dimethyl)glycylamino, and ethoxythiocarbonylthio; and

General Formula (IV)

Structure O

or

Structure P

70 wherein: R7, R8, and R9 taken together in each case, have the following meanings:

	R7	R8	R9
	amino	hydrogen	hydrogen
	nitro	hydrogen	hydrogen
	azido	hydrogen	hydrogen
75	dimethylamino	hydrogen	azido
	hydrogen	hydrogen	amino
	hydrogen	hydrogen	azido
	hydrogen	hydrogen	nitro
	bromo	hydrogen	hydrogen
80	dimethylamino	hydrogen	amino
	acylamino	hydrogen	hydrogen
	hydrogen	hydrogen	acylamino
	amino	hydrogen	nitro
	hydrogen	hydrogen	(N,N-dimethyl)glycylamino
85	amino	hydrogen	amino
	diethylamino	hydrogen	hydrogen
	hydrogen	hydrogen	ethoxythiocarbonylthio
	dimethylamino	hydrogen	methylamino
	dimethylamino	hydrogen	acylamino
90	dimethylamino	chloro	amino
	amino	chloro	amino
	acylamino	chloro	acylamino
	hydrogen	chloro	amino
	amino	chloro	hydrogen
95	acylamino	chloro	hydrogen
	mono alkyl amino	chloro	amino
	nitro	chloro	amino

and pharmaceutically acceptable and unacceptable salts thereof.

18. A method of treating cataract formation in a mammal comprising administering to the mammal an effective amount of a tetracycline derivative.

19. A method according to Claim 18, wherein said tetracycline derivative is a non-antimicrobial tetracycline.

20. A method according to Claim 18, wherein said tetracycline derivative is a dedimethylaminotetracycline.

21. A method according to Claim 20, wherein said dedimethylaminotetracycline is selected from the group consisting of 4-dedimethylaminotetracycline, 4-dedimethylamino-5-oxytetracycline, 4-dedimethylamino-7-chlorotetracycline, 4-hydroxy-4-dedimethylaminotetracycline, 5a,6-anhydro-4-hydroxy-4-dedimethylaminotetracycline, 6 α -deoxy-5-hydroxy-4-dedimethylaminotetracycline, 6-demethyl-6-deoxy-4-dedimethylaminotetracycline, 4-dedimethylamino-12a-deoxytetracycline, 12 α -deoxy-4-deoxy-4-dedimethylaminotetracycline, 12a, 4 α -anhydro-4-dedimethylaminotetracycline, 7-dimethylamino-6-demethyl-6-deoxy-4-dedimethylaminotetracycline, 5-hydroxy-6- α -deoxy-4-dedimethylaminotetracycline, 4-dedimethylamino-12 α -deoxyanhydrotetracycline and 4-dedimethylamino-11-hydroxy-12a-deoxytetracycline.

22. A method according to Claim 18, wherein said tetracycline derivative is 6 α -deoxy 5-hydroxy 4-dedimethylamino tetracycline.

23. A method according to Claim 18, wherein said tetracycline derivative is selected from the group consisting of 6a-benzylthiomethylenetetracycline, tetracyclinoitrile, the mono-N-alkylated amide of tetracycline, 6-fluoro-6-demethyltetracycline, 11a-chlorotetracycline, tetracycline pyrazole, and 12a-deoxytetracycline and its derivatives.

24. A method according to Claim 18, wherein said tetracycline derivative is an antimicrobial tetracycline.

25. A method according to Claim 24, wherein said tetracycline derivative is tetracycline.

26. A method according to Claim 24, wherein said tetracycline derivative is minocycline.

27. A method according to Claim 24, wherein said tetracycline derivative is doxycycline.

28. A method according to Claim 18, wherein said tetracycline derivative is administered systemically.

29. A method according to Claim 28, wherein said tetracycline derivative is administered systemically by a controlled release delivery system.

30. A method according to Claim 18, wherein said tetracycline derivative is administered orally.

31. A method according to Claim 18, wherein said tetracycline derivative is administered topically.

32. A method according to Claim 18, wherein said tetracycline derivative is a tetracycline compound of the formulae:

Structure A or Structure B or
Structure C or Structure D

5 wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

10 R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;

R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, diazonium, di(lower alkyl)amino and $RCH(NH_2)CO$;

15 R is hydrogen or lower alkyl; and pharmaceutically acceptable and unacceptable salts thereof; with the following provisos:

when either R7 and R9 are hydrogen then R8 must be halogen; and

when R6-a, R6, R5 and R9 are all hydrogen and R7 is hydrogen, amino, nitro,

halogen, dimethylamino or diethylamino, then R8 must be halogen; and

when R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is hydrogen, amino, nitro, halogen or diethylamino, then R8 is halogen; and

when R6-a is methyl, R6 is hydroxyl, R5, R7 and R9 are all hydrogen, then R8
5 must be halogen; and

when R6-a, R6 and R5 are all hydrogen, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

when R6-a is methyl, R6 is hydrogen, R5 is hydroxyl, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

10 when R6-a is methyl, R6, R5 and R9 are all hydrogen and R7 is cyano, then R8 must be halogen.

33. A method according to Claim 18, wherein said tetracycline derivative is a tetracycline compound of the formulae:

Structure E	or	Structure F or
Structure G	or	Structure H

5 wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, and di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

10 R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;

R4 is selected from the group consisting of NOH, N-NH-A, and NH-A, where A is a lower alkyl group;

R8 is selected from the group consisting of hydrogen and halogen;

15 R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, di(lower alkyl)amino and $RCH(NH_2)CO$;

R is hydrogen or lower alkyl; and pharmaceutically acceptable and unacceptable salts thereof; with the following provisos:

when R4 is NOH, N-NH-alkyl or NH-alkyl and R7, R6-a, R6, R5, and R9 are
 20 all hydrogen, then R8 must be halogen; and

when R4 is NOH, R6-a is methyl, R6 is hydrogen or hydroxyl, R7 is halogen,
 R5 and R9 are both hydrogen, then R8 must be halogen; and

when R4 is N-NH-alkyl, R6-a is methyl, R6 is hydroxyl and R7, R5, R9 are all
 hydrogen, then R8 must be halogen; and

25 when R4 is NH-alkyl, R6-a, R6, R5 and R9 are all hydrogen, R7 is hydrogen,
 amino, mono(lower alkyl)amino, halogen, di(lower alkyl)amino or hydroxyl, then R8
 must be halogen; and

when R4 is NH-alkyl, R6-a is methyl, R6 and R9 are both hydrogen, R5 is
 hydroxyl, and R7 is mono(lower alkyl)amino or di(lower alkyl)amino, then R8 must
 30 be halogen; and

when R4 is NH-alkyl, R6-a is methyl, R6 is hydroxy or hydrogen and R7, R5,
 and R9 are all be hydrogen, then R8 must be halogen.

34. A method according to Claim 18, wherein said tetracycline derivative
 is a 4-dedimethylaminotetracycline compound having general formulae (I) through
 (IV):

General Formula (I)

5

Structure I

wherein: R7, R8, and R9 taken together in each case, have the following meanings:

	R7	R8	R9
	azido	hydrogen	hydrogen
	dimethylamino	hydrogen	azido
10	hydrogen	hydrogen	amino
	hydrogen	hydrogen	azido
	hydrogen	hydrogen	nitro
	dimethylamino	hydrogen	amino
	acylamino	hydrogen	hydrogen
15	hydrogen	hydrogen	acylamino
	amino	hydrogen	nitro
	hydrogen	hydrogen	(N,N-dimethyl)glycylamino
	amino	hydrogen	amino
	hydrogen	hydrogen	ethoxythiocarbonylthio
20	dimethylamino	hydrogen	acylamino
	dimethylamino	hydrogen	diazonium

25	dimethylamino	chloro	amino
	hydrogen	chloro	amino
	amino	chloro	amino
	acylamino	chloro	acylamino
	amino	chloro	hydrogen
	acylamino	chloro	hydrogen
30	mono alkylamino	chloro	amino
	nitro	chloro	amino
	dimethylamino	chloro	acylamino
	dimethylamino	chloro	dimethylamino

and

General Formula (II)

35	Structure J	or	Structure K or
	Structure L	or	Structure M

wherein: R7, R8, and R9 taken together in each case, have the following meanings:

	R7	R8	R9
40	azido	hydrogen	hydrogen
	dimethylamino	hydrogen	azido
	hydrogen	hydrogen	amino
	hydrogen	hydrogen	azido
	hydrogen	hydrogen	nitro
	dimethylamino	hydrogen	amino
45	acylamino	hydrogen	hydrogen
	hydrogen	hydrogen	acylamino
	amino	hydrogen	nitro
	hydrogen	hydrogen	(N,N-dimethyl)glycylamino
	amino	hydrogen	amino
	hydrogen	hydrogen	ethoxythiocarbonylthio
50	dimethylamino	hydrogen	acylamino
	hydrogen	hydrogen	diazonium
	hydrogen	hydrogen	dimethylamino
	diazonium	hydrogen	hydrogen
	ethoxythiocarbonylthio	hydrogen	hydrogen
	dimethylamino	chloro	amino
55	amino	chloro	amino
	acylamino	chloro	acylamino
	hydrogen	chloro	amino
	amino	chloro	hydrogen
	acylamino	chloro	hydrogen
60			

mono alkyl amino
nitro
and
chloro
chloro
amino
amino

General Formula (III)

65

Structure N

wherein: R8 is hydrogen or halogen and R9 is selected from the group consisting of nitro, (N,N-dimethyl)glycylamino, and ethoxythiocarbonylthio; and

General Formula (IV)

70

Structure O

or

Structure P

wherein: R7, R8, and R9 taken together in each case, have the following meanings:

75

R7
amino
nitro
azido
dimethylamino
hydrogen
hydrogen
hydrogen
bromo
dimethylamino
acylamino
hydrogen

R8
hydrogen
hydrogen
hydrogen
hydrogen
hydrogen
hydrogen
hydrogen
hydrogen
hydrogen
hydrogen
hydrogen
hydrogen

R9
hydrogen
hydrogen
hydrogen
azido
amino
azido
nitro
hydrogen
amino
hydrogen
acylamino
nitro

80

amino
hydrogen
amino
diethylamino
hydrogen
dimethylamino
dimethylamino
dimethylamino
amino
acylamino
hydrogen
amino

hydrogen
hydrogen
hydrogen
hydrogen
hydrogen
hydrogen
hydrogen
hydrogen
hydrogen
chloro
chloro
chloro
chloro
chloro

(N,N-dimethyl)glycylamino
amino
hydrogen
ethoxythiocarbonylthio
methylamino
acylamino
amino
amino
acylamino
amino
hydrogen

85

90

95

acylamino
mono alkyl amino
nitro

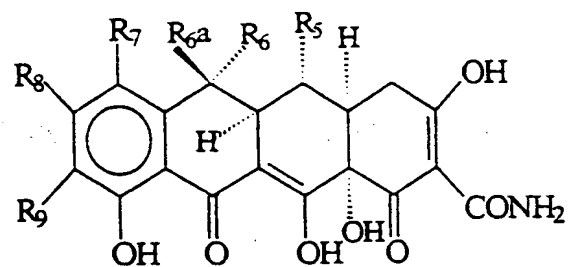
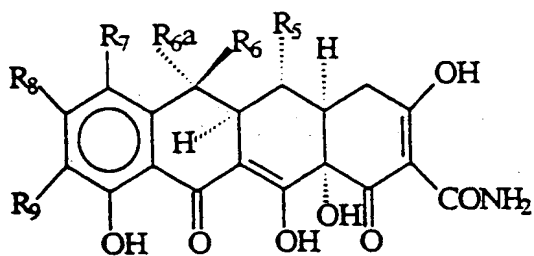
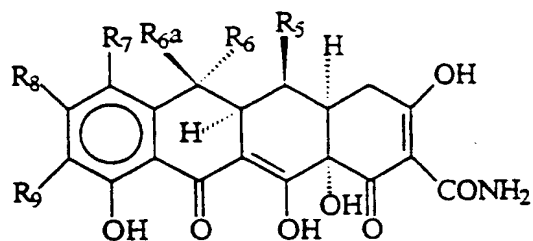
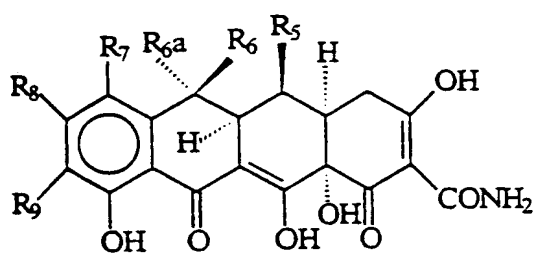
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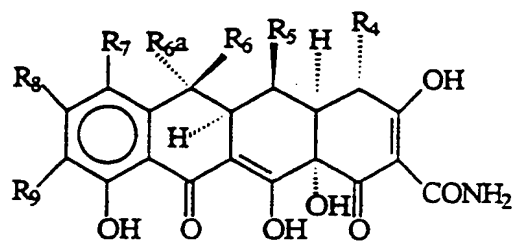
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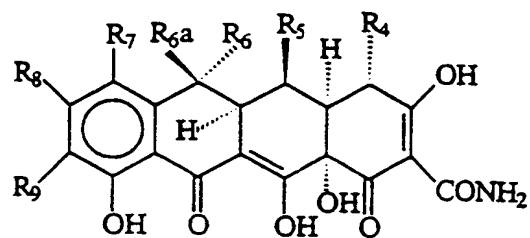
and pharmaceutically acceptable and unacceptable salts thereof.

STRUCTURES A-P

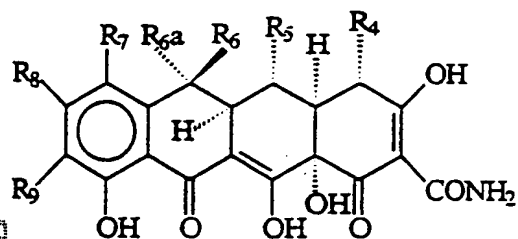




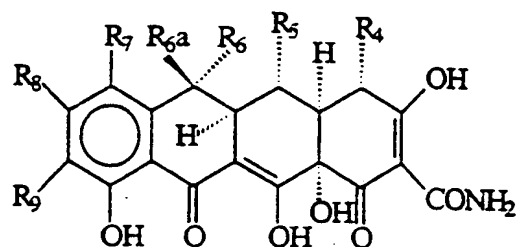
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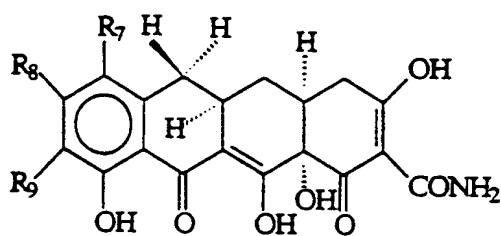
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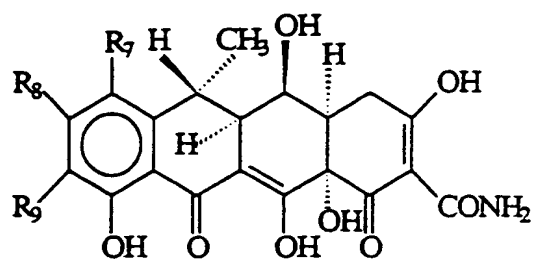
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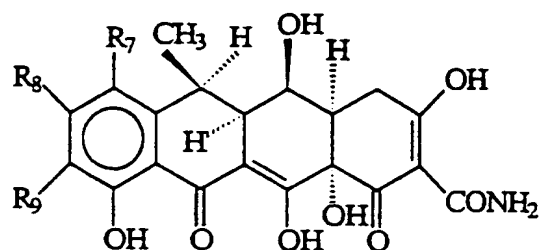
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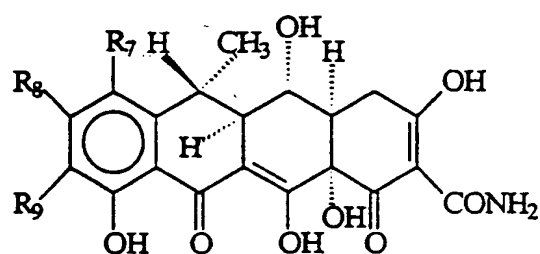
Structure I



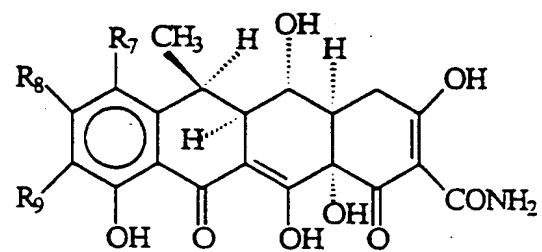
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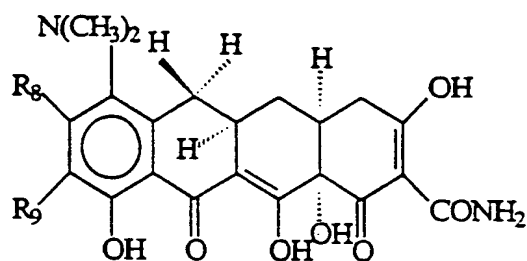
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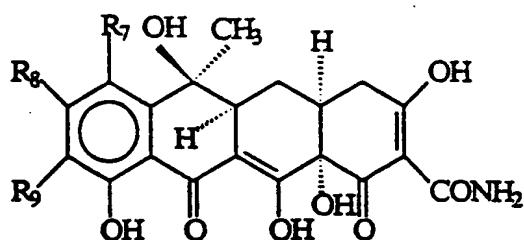
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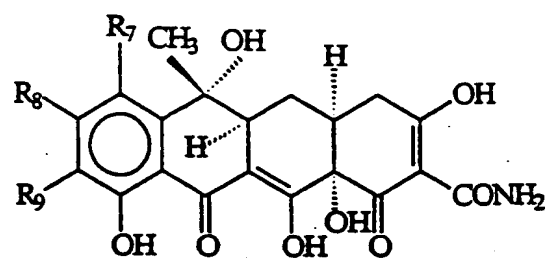
Structure M



Structure N



Structure O



Structure P